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PATENT, TRADEMARK
AND COPYRIGHT CAUSES

703-521-2110

December 28, 1983

Dr. G. Esler Inskeep
Philip Morris Research Center
P. O. Box 26583
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Re: United States Patent Application Serial
Number 377,989, filed May 13, 1982,
entitled OPTICALLY ACTIVE NICOTINE ANALOGS
AND PROCESS FOR THEIR PREPARATION of
Edwards III
Your Reference: PM 893
Our Reference: D&O-79-14/II

Dear Les:

This is further to your letter of December 8th and a recent phone conference with W. Edwards.

In the present case, claims 40-47 are rejected, and claims 48-55 are allowed. Our opinion concerning rejected claims 40-47 is summarized as follows.

Claims 40-43 are rejected over the Castonguay et al reference which discloses 3-(hydroxymethyl)-1-methyl-2-(3-pyridyl)pyrrolidine (Compound 16), which is a position isomer of the claims 40-43 4-hydroxymethyl-1-methyl-2-(3-pyridyl)pyrrolidine compound. There is essentially no prospect that claims 40-43 will be allowed without comparative data which demonstrate an unexpected difference in properties between the two position isomers. W. Edwards has advised us that no further laboratory effort will be authorized.

Claims 44-47 are either anticipated or rendered obvious by the Titus et al and C. A. Formula Index disclosures. These references recite "hydroxynicotine", which is a generic description of the claims 44-47 compounds. Note also that U.S. 3,644,176 discloses 6-hydroxynicotine.

Claims 44-47 are rejected further over the homolog compound disclosed in Hecht et al, i.e., the reference compound lacks a 2-methyl substituent.

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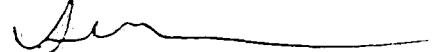
As it is apparent, to achieve allowance of claims 44-47 requires an extensive laboratory undertaking, with no certainty that the comparative data would support a showing that the properties of "hydroxynicotine" isomeric compounds differ from each other in an unexpected manner, and also differ from "hydroxynornicotine" isomers. Since no comparative data is forthcoming, we cannot succeed in overcoming a *prima facie* basis of rejection.

Although the foregoing opinion is disappointing to the inventor, we do have claims 48-55 allowed in this case, as well as claims 1-24 in S.N. 229,481 (D&O-79-14) and claims 33, 35-36, 38-39 and 56 in S.N. 377,990 (D&O-79-14/I).

During our telephone conversation with W. Edwards, I had suggested that a meeting might be helpful. However, upon further study of the rejections and the lack of comparative data, I feel we have gone as far as possible.

Very truly yours,

DEPAOLI & O'BRIEN, P.C.



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